

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/05943

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims <u>(Please See supplemental sheet)</u>	YES
	Claims <u>(Please See supplemental sheet)</u>	NO
Inventive Step (IS)	Claims <u>(Please See supplemental sheet)</u>	YES
	Claims <u>(Please See supplemental sheet)</u>	NO
Industrial Applicability (IA)	Claims <u>(Please See supplemental sheet)</u>	YES
	Claims <u>(Please See supplemental sheet)</u>	NO

**2. citations and explanations (Rule 70.7)**

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by WO 98/36639 (Ultradent Products). The reference discloses that the compound bis-glycerol methacrylate phosphate is useable as a polymerizable adhesion monomer in dental compositions.

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by JP 5-311200 (Nagayama). The reference purportedly describes bis(3-(2-ethylpentyl)oxy-2-hydroxy-1-propyl)phosphate as a detergent additive.

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by JP 57-167364 (Sankin Industry). The reference teaches that bis(3-methacryloyloxy-2-chloro-1-propyl)phosphate is useful in dental and bone cements as an polymerizable adhesion monomer.

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by JP 49-002266 (Hosoda). The reference teaches that bis(3-(2-propenyl)oxy-2-hydroxy-1-propyl)(phosphate) is useful in compositions applied to steel as a blackening agent.

Claim 5 lacks novelty under PCT Article 33(2) as being anticipated by JP 58-10559 (Okumura). The reference discloses methyl 2-chloro-3-sulfothiopropanoate as an intermediate in the synthesis of cysteine.

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by JP 63-265972 (Tagashira et al.). The reference teaches that ammonium bis-glycerol methacrylate phosphate is useable in adhesive formulations.

Claims 1 and 2 lack novelty under PCT Article 33(2) as being anticipated by U.S. Patent No. 4,504,409 (Tsutsumi et al.). The reference describes a class of compounds that includes bis(3-hydrocarboxy-2-hydroxy-1-propyl)phosphate and specifically bis(3-dodecyloxy-2-hydroxy-1-propyl)phosphate and bis(3-(Continued on Supplemental Sheet.)

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): A61K 31/255, 31/66; C07F 9/09; C07C 305/10, 305/06 and US Cl.: 514/120, 125, 129, 517; 558/32, 34, 179, 182, 183, 186, 188

**I. BASIS OF REPORT:**

5. (Some) amendments are considered to go beyond the disclosure as filed:

NONE

**V. 1. REASONED STATEMENTS:**

The report as to Novelty was positive (YES) with respect to claims 3, 4 and 6-57.

The report as to Novelty was negative (NO) with respect to claims 1, 2 and 5.

The report as to Inventive Step was positive (YES) with respect to claims 4,6,7,10,11,16,17,19,23-27,33 and 35-57.

The report as to Inventive Step was negative (NO) with respect to claims 1,2,3,5,8,9,12-15,18,20-22,28-32 and 34.

The report as to Industrial Applicability was positive (YES) with respect to claims 1-57.

The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

octadecyloxy-2-hydroxy-1-propyl)phosphate; note column 3, formulae (d) and (e).

Claims 1,2,3,5,8,9,12-15,18,20-22,28-32 and 34 lack an inventive step under PCT Article 33(3) as being obvious over U.S. Patent No. 4,504,409 (Tsutsumi et al.).

This invention relates to a broad class of organophosphate diesters that includes bis(3-hydrocarbyloxy-2-hydroxy-1-propyl)phosphates. The compounds are alleged to be useful to treat apoptosis and dermatological conditions such as wrinkling and hair loss. The reference describes this class of compounds and teaches that they can be used as emulsifying agents exhibiting low irritation to skin. This invention lacks inventive step because the person having ordinary skill in the art would have been motivated to prepare them for use in personal care products where their property of manifesting reduced irritation would make them desirable, for example, for use in cosmetics. In column 4, line 48, through column 5, line 16, other compounding ingredients are described that are consistent with use in cosmetics. These include surfactants, fats, vitamins, and antimicrobials.

Claims 4,6,7,10,11,16,17,19,23-27,33 and 35-57 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest compositions of the compounds of claim 1 with PEG or proteins, or methods of use wherein the compounds are administered to treat apoptosis or apoptosis-related disorders.

Claims 1-57 meet the criteria set out in PCT Article 33(4) because the compounds have industrial applicability as pharmacological agents for the treatment of apoptosis or apoptosis-related disorders.

**----- NEW CITATIONS -----**

none



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61K 31/255, 31/66, C07F 9/09, C07C 305/10, 305/06</b>		A3	(11) International Publication Number: <b>WO 99/47101</b>
			(43) International Publication Date: 23 September 1999 (23.09.99)
(21) International Application Number: PCT/US99/05943 (22) International Filing Date: 17 March 1999 (17.03.99)  (30) Priority Data: 60/078,375 18 March 1998 (18.03.98) US			(74) Agents: BROWN, Theresa, A. et al.; Sheridan Ross P.C., Suite 3500, 1700 Lincoln Street, Denver, CO 80203-4501 (US).
(71) Applicants (for all designated States except US): LXR BIOTECHNOLOGY, INC. [US/US]; 1401 Marina Way South, Richmond, CA 94804 (US). OXFORD ASYMMETRY LIMITED [GB/GB]; 151 Milton Park, Abingdon, Oxfordshire LX14 4SD (GB).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(72) Inventors; and (75) Inventors/Applicants (for US only): GODDARD, John, G. [CA/US]; 110 Congo Street, San Francisco, CA 94131 (US). PICKER, Donald, H. [US/US]; One Springfield Avenue, Summit, NJ 07901 (US). UMANSKY, Samuil, R. [RU/US]; 6034 Monterey Avenue, Richmond, CA 94805 (US). PRICE, Steven [GB/GB]; 25 Eskdale Road, Stoke Mandeville, Aylesbury, Bucks HP22 5UJ (GB). WIJKMANS, Jacobus, C., H., M. [GB/GB]; 30 Alexander Close, Abingdon, Oxon OX14 1XA (GB). BOYD, Edward, Andrew [GB/GB]; 61 Tamar Way, Didcot, Oxon OX11 7QH (GB). BAXTER, Anthony, David [GB/GB]; 1 Kingfisher Close, Abingdon, Oxon OX14 5NP (GB).			<p><b>Published</b>  <i>With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
(54) Title: COMPOSITIONS CONTAINING LYSOPHOSPHATIDIC ACIDS WHICH INHIBIT APOPTOSIS AND USES THEREOF			
(57) Abstract <p>The invention provides anti-apoptotic compositions containing lysophosphatidic acids and methods for making and using the compositions. Such compositions can also contain LPA potentiating agents, including proteins, lipid membrane structures and polymers such as polyethylene glycols. The compositions can additionally contain other pharmaceutically effective agents such as drugs, antibiotics, wound healing agents and antioxidants.</p>			

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EE	Estonia	LR	Liberia	SG	Singapore		

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/05943

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/255, 31/66; C07F 9/09; C07C 305/10, 305/06  
US CL :514/120, 125, 129, 517; 558/32, 34, 179, 182, 183, 186, 188

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/120, 125, 129, 517; 558/32, 34, 179, 182, 183, 186, 188

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN International®, REGISTRY Database, Accessed 22 June 1999, Structure-based Search Query

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	WO 98/36639 A1 (ULTRADENT PRODUCTS, INC.) 27 August 1998, page 6, first full paragraph.	1
X	JP 05-311200 A2 (NAGAYAMA) 22 November 1993, page 776, formula 2.	1
X	JP 63-265972 A2 (TAGASHIRA et al.) 02 November 1988, page 517, column 1.	1
X	JP 57-167364 A2 (SANKIN INDUSTRY CO.) 15 October 1992, page 513, column 1.	1
X	JP 49-002266 B4 (HOSODA) 19 January 1974, page 108, compound 3.	1
X	JP 58-010559 A2 (AJINOMOTO CO., INC.) 21 January 1983, page 479, column 1, also the table on page 481.	5

Further documents are listed in the continuation of Box C.  See patent family annex.

* Special categories of cited documents:	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A*		document defining the general state of the art which is not considered to be of particular relevance
*E*	*X*	earlier document published on or after the international filing date
*L*		document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
*O*	*Y*	document referring to an oral disclosure, use, exhibition or other means
*P*	*&*	document published prior to the international filing date but later than the priority date claimed

Date of the actual completion of the international search

28 JUNE 1999

Date of mailing of the international search report

30 SEP 1999

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

MICHAEL G. AMBROSE

Telephone No. (703) 308-1235

M/1

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

## Date of mailing (day/month/year)

10 March 2000 (10.03.00)

## International application No.

PCT/US99/05943

## International filing date (day/month/year)

17 March 1999 (17.03.99)

To:  
Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Applicant's or agent's file reference  
4147-10-PCT

## Priority date (day/month/year)

18 March 1998 (18.03.98)

## Applicant

GODDARD, John, G. et al



## 1. The designated Office is hereby notified of its election made:

 in the demand filed with the International Preliminary Examining Authority on:

15 October 1999 (15.10.99)

 in a notice effecting later election filed with the International Bureau on:

---

2. The election  was was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Sean Taylor

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

Date of mailing (day/month/year)

10 March 2000 (10.03.00)

To:

Invention Office of the Democratic  
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Republic of Korea  
Kinmaul 1 dong, Bip'a Street,  
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DE CORÉE

in its capacity as elected Office

International application No.

PCT/US99/05943

Applicant's or agent's file reference

4147-10-PCT

International filing date (day/month/year)

17 March 1999 (17.03.99)

Priority date (day/month/year)

18 March 1998 (18.03.98)

Applicant

LXR BIOTECHNOLOGY, INC. et al \*

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

15 October 1999 (15.10.99)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
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Facsimile No.: (41-22) 740.14.35

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## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4147-10-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/05943	International filing date (day/month/year) 17 MARCH 1999	Priority date (day/month/year) 18 MARCH 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant LXR BIOTECHNOLOGY, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 15 OCTOBER 1999	Date of completion of this report 14 JULY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  MICHAEL G. AMBROSE
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/05943

## L Basis of the report

## 1. With regard to the elements of the international application:\*

 the international application as originally filed the description:

pages 1-89

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of the claims:

pages 90-96

pages NONE

pages NONE

pages NONE

, as originally filed  
, as amended (together with any statement) under Article 19  
, filed with the demand  
, filed with the letter of the drawings:

pages 1-15

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of the sequence listing part of the description:

pages NONE

pages NONE

pages NONE

, as originally filed  
, filed with the demand  
, filed with the letter of

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4.  The amendments have resulted in the cancellation of: the description, pages NONE the claims, Nos. NONE the drawings, sheets/fig. NONE5.  This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/05943

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,504,409 A (TSUTSUMI et al.) 12 March 1985, formula I in column 2, also column 3.	1, 2